IN VITRO STUDIES OF SOME SALMONELLA ORGANISMS MADE RESISTANT TO STREPTOMYCIN

BY

MURRAY SAM COOPER

B.S., City College of New York, 1947
M.S., University of Illinois, 1948

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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R. UNIV. BIBLIOTHEEK LEIDEN

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Introduction

One of the most important antibiotics in use today is streptomycin. It was discovered by Schatz, Bugie and Waksman (1944).

Streptomycin is an important addition to chemotherapy. In a review, Keefer (1949) noted that streptomycin is active against many sulfonamide and penicillin-resistant infections. It may be considered a wonder drug, yet like penicillin it has many shortcomings. Molitor and Graessle (1946) found that under certain conditions the toxicity of streptomycin is important.

Development of resistance to streptomycin is also important in chemotherapy. Miller and Bohnhoff (1949) concluded that bacteria develop resistance to streptomycin more rapidly than to penicillin. Pratt and Dufrenoy (1949) claimed that streptomycin-resistant organisms generally have undiminished virulence, while a loss in virulence usually accompanies penicillin resistance.

Development of resistance to antibiotics is of interest as a basic biological phenomenon and the problem of resistance to streptomycin is of practical importance. This investigation deals with resistance to antibiotics as observed in some Salmonella organisms made resistant to streptomycin *in vitro*.

Experimental and Results

Some Salmonellas and other gram negative bacteria were made resistant to streptomycin *in vitro*. The differences between these streptomycin-resistant variants and their parent

streptomycin-sensitive strains were studied in these experiments.

The following strains were used:

Number of strains used	*Name*
1	*Salmonella choleraesuis* var. *Kunzendorf*
2	*Salmonella pullorum*
3	*Salmonella derby*
1	*Salmonella anatis*
1	*Salmonella typhosa*
1	*Salmonella typhimurium*

A decrease in gas production in carbohydrate broth was observed in 6 of the 9 resistant variants compared to the parent sensitive strains.

No blackening was noted in lead acetate agar by 5 of the 9 resistant variants. All but one of the sensitive parent strains caused blackening in lead acetate agar. Less blackening was produced on Kligler's Iron agar by 7 of the 9 resistant variants. The sensitive parent strains all caused blackening in Kligler's Iron agar. These results indicate that some of the streptomycin-resistant organisms lost part of their ability to liberate H_2S from proteins and their products.

One of the resistant strains of Salmonella had no flagellar antigens. The serological typing of this organism was not possible. Streptomycin was not destroyed when some resistant organisms grew in its presence. Growth in tryptone broth was decreased for 5 of 9 streptomycin-resistant organisms compared to their parent sensitive strains. Streptomycin in a concentration of 1500 micrograms per milliliter decreased the growth of 4 of 9 resistant strains in tryptone compared to the growth of these resistant variants in tryptone without streptomycin.

Those streptomycin-resistant strains tested did not have a greater tolerance for reduced surface tension than their parent sensitive strains.

Gas production from dextrose was studied for resting cells of some streptomycin-resistant Salmonellas. The manometric techniques employed were after Umbreit et al (1949) and Woods and Clifton (1937). A decrease in Q_{H_2} was noted for 3 of 9 resistant strains and a decrease in Q_{CO_2} was observed for 5 of 9 resistant strains compared to the relative values for their parent sensitive strains.

Growth in Difco Brain Heart Infusion broth was studied for some streptomycin-resistant Salmonellas. A longer lag phase and less final growth was noticed for 6 of the 9 resistant variants compared to their parent strains.

The ability of a resting cell suspension to produce acid in a dextrose solution was studied for some streptomycin-resistant organisms. It was noted that 4 of 9 resistant variants produced less of a decrease in pH than their parent strains.

The effect of streptomycin on the aerobic respiration of *Salmonella typhosa* strain Hopkins was studied. It was found that this organism oxidized dextrose at a faster rate when streptomycin was added. Decreases in oxygen uptake were observed for asparagin and sodium lactate when streptomycin was added.

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VITA

The author was born January 14, 1923 in Poland. He came to the United States in 1929 and attended public schools in New York City. In 1940 he entered the College of the City of New York. He left school in 1943 for active duty with the U. S. Army for three years. During this time he served with an Infantry division in Europe. After separation from military service, he returned to the same institution and received his Bachelor of Science degree in 1947. He then entered the University of Illinois and received his Master of Science degree in Bacteriology in 1948. In February 1948 the author married Claire Sandberg. After six months in industry, he returned to the University of Illinois to begin studies towards his Doctor of Philosophy degree in Bacteriology. During his third year he held a University fellowship.

He is a member of Sigma Xi and the Society of American Bacteriologists.

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